United States District Court
District of Massachusetts

IN RE: FRESENIUS GRANUFLO/ NAUTRALYTE DIALYSATE PRODUCTS LIABILITY LITIGATION	MDL No. 13-2428
This document relates to:	
Gloria Cothern Dunaway Case No. 13-11714	
Mervin Boyd Case No. 13-11717	
Michael McNulty Case No. 13-12403	
Charles Cameron Case No. 13-12446	
Daniel Carter Case No. 13-12459	
Joyce Marie Clark Case No. 13-12460	
Kathy Dennis Case No. 13-12467	
Kimberly Ross Case No. 13-12478	
Beulah Williams Case No. 13-12486	
Sophia Walker Case No. 13-12487	
Janice McGhee Case No. 13-13172	
Max Riben Case No. 15-11134	
Josephine Gallardo Hernandez Case No. 18-11224	

MEMORANDUM & ORDER

GORTON, J.

This Multi-District Litigation arises from the use of acid concentrates in the treatment of dialysis patients who died following the procedures. The acid concentrates at issue, NaturaLyte and GranuFlo, are manufactured by the defendants Fresenius Medical Care Holdings, Inc. d/b/a Fresenius Medical Care North America; Fresenius USA, Inc.; Fresenius USA Manufacturing, Inc.; and Fresenius USA Marketing, Inc. (collectively "Fresenius"). All of the defendants move for summary judgment on the claims of certain opt-out plaintiffs.

Here, the Court addresses Fresenius's motions for summary judgment based on 1) lack of evidence of elevated serum bicarbonate levels, 2) lack of evidence of causation 3) claims involving Naturalyte and 4) the learned intermediary doctrine.

Subject to the motion related to elevated serum bicarbonate levels are the following plaintiffs: Gloria Cothern Dunaway, Mervin Boyd, Michael McNulty, Daniel Carter, Joyce Marie Clark, Kimberly Ross, Beulah Williams, Sophia Walker, Janice McGhee and Max Riben. Subject to the motion related to the lack of evidence of causation are the following plaintiffs: Gloria Cothern Dunaway, Mervin Boyd, Michael McNulty, Daniel Carter, Joyce Marie Clark, Kathy Dennis, Kimberly Ross, Sophia Walker,

Janice McGhee, Max Riben and Josephine Gallardo Hernandez. Subject to the motion involving Naturalyte are the following plaintiffs: Charles Cameron, Daniel Carter, Sophia Walker, Max Riben and Josephine Gallardo Hernandez. All remaining 13 plaintiffs are subject to the learned intermediary doctrine motion.

Because there are no outstanding genuine issues of material fact, the Court will allow the motions for summary judgment as against all pertinent plaintiffs.

I. Background

A. Factual Background

1. The Second Amended Complaint & Plaintiffs' General Causation Theory

Plaintiffs' complaint is premised on the theory that Fresenius failed to warn doctors about how to use GranuFlo and NaturaLyte safely with their hemodialysis patients. According to plaintiffs, the acetate in GranuFlo and NaturaLyte leads to a "dangerous increase" in serum bicarbonate levels in patients undergoing hemodialysis which results in metabolic alkalosis triggering cardiac arrest and sudden cardiac death. In particular, plaintiffs allege that alkalosis

> is caused by too much bicarbonate in the blood [and that it is those patients with] elevated bicarbonate levels in their blood

who are at an increased risk of sudden cardiac arrest. Plaintiffs contend that Fresenius should therefore have advised doctors to

> pay attention to the increase in serum bicarbonate levels [and to] reduce the amount of bicarbonates being delivered . . . during dialysis to take into account the additional bicarbonate from NaturaLyte and/or GranuFlo.

2. Facts Applicable to All Serum Bicarbonate Plaintiffs

Ray Hakim, MD, former Chief Medical Officer for Fresenius Medical Services, authored a memorandum dated November 4, 2011 ("the Hakim Memo") that was addressed to medical directors and attending physicians regarding the subject of "Dialysate Bicarbonate, Alkalosis and Patient Safety." The Hakim Memo discussed the results of a "case-control study" that

> evaluated risk factors in [hemodialysis] patients who suffered from [cardiopulmonary] arrest in the facility . . . compared to other [hemodialysis] patients . . . within the same facilities between January 1, and December 31, 2010.

The data in the Hakim Memo depicted no statistically significant increased risk of in-center cardiopulmonary arrest for patients with pre-dialysis serum bicarbonate levels in the mid to low 20s. When focusing on bicarbonate levels alone, patients with a pre-dialysis serum bicarbonate level of 28 milliequivalents ("mEq/L") or more were depicted as having the greatest relative

risk for cardiopulmonary arrest during dialysis as compared to other groups and no other group was marked with a statistically significant increased risk. When pre-dialysis potassium lab values were included in the analysis, patients with a pre-dialysis serum bicarbonate value under 28 mEq/L and potassium greater than or equal to four mEq/L had no increased risk. Dr. Hakim testified that an earlier draft of the Hakim Memo defined alkalosis as "pre-dialysis bicarbonate of greater than or equal to 28 milliequivalents," but that language was not included in the final version of the memo.

Plaintiffs retained Dr. Derek Fine, as an expert witness on general and specific causation in this litigation. He is an Associate Professor of Medicine at Johns Hopkins University School of Medicine and has a clinical practice that includes treating dialysis patients at a DaVita outpatient dialysis unit in Baltimore, Maryland. Dr. Fine testified during his deposition that a "normal" range for pre-dialysis serum bicarbonate is subject to "varying opinion" but that he would

> like to see the [serum] bicarb[onate] somewhere between, in most cases, 20 and 24 [mEq/L] [and that he would tell his fellows and nurse practitioners that the] K/DOQI guidelines say greater than 22 [mEq/L] is a reasonable target.

Dr. Fine also testified that if he were asked to place an "upper limit" for pre-dialysis serum bicarbonate, that number would be

27 mEq/L. Dr. Fine testified that, in general, it is unnecessary to adjust a bicarbonate prescription because most patients are not alkalotic, so the key is to ensure his nephrology physician fellows are aware "that alkalosis is bad." He further testified that studies show that "high [serum] bicarb[onate] is bad" and "associated with mortality" and "sudden cardiac arrest." His expert report notes that "normal" serum bicarbonate levels are 22 to 26 mEq/L for arterial blood and 23 to 27 mEq/L for venous blood.

Plaintiffs also retained Dr. Sushrut Waikar, as an expert witness on general and specific causation in this litigation. Dr. Waikar is an Associate Professor of Medicine at Harvard Medical School and he treats nephrology patients, including some who are on dialysis, at Brigham & Women's Hospital in Boston, Massachusetts. At his deposition, Dr. Waikar testified that the typical serum bicarbonate range is 20 to 26 mEq/L and the range he targets for his own patients' pre-dialysis serum bicarbonate levels is "22 to 26 [mEq/L], around there, would be reasonable, maybe 22 to 24 [mEq/L]." Dr. Waikar also testified that he would adjust the bicarbonate prescription for a patient based on

> [t]he presence or absence of chronic obstructive pulmonary disease, the presence or absence of severe metabolic alkalosis or acidosis.

When asked to explain what he meant by a patient presenting with metabolic alkalosis, Dr. Waikar gave the example of a patient with a serum bicarbonate concentration level of 35 mEq/L when he comes into the dialysis unit. He was also asked to explain what he meant when he referred to "significant alkalosis," and he gave examples of a patient with serum bicarbonate levels of 30 or 35 mEq/L.

The third expert witness on general causation retained by plaintiffs is Dr. David Goldfarb. He is a professor at New York University and treats dialysis patients at a Veterans Affairs unit in the New York Harbor Healthcare System. In discussing bicarbonate levels that would be a potential cause for concern, Dr. Goldfarb agreed that levels below 22 mEq/L are "associated with adverse outcomes," as are bicarbonate levels of 28 or 30 or 35 mEq/L. He also testified that in his dialysis practice, he gives his patients 35 mEq/L of bicarbonate and that none of the treating nephrologists in the chronic dialysis unit prescribes different levels of bicarbonate. In fact, Dr. Goldfarb indicated that 1) his recommendation would be not to change the bicarbonate prescription for any of the chronic kidney disease patients at the New York Harbor clinic and 2) he never adjusts the prescription for treatment based on pre or post-dialysis serum bicarbonate values.

Finally, plaintiffs retained Dr. Steven C. Borkan, as a fourth expert witness on general and specific causation. Dr. Borkan is a professor at Boston University and maintains an active clinical nephrology practice in facilities affiliated with DaVita. During his June, 2015 deposition, Dr. Borkan testified that his "target" pre-dialysis serum bicarbonate range for his own patients is between 22 and 24 mEq/L. At his October, 2015 deposition, he added that he does not

> dial back the bicarbonate delivered in prescription [to his own patients unless the patient] has a predialysis bicarbonate level that's above 24 [mEq/L].

Dr. Borkan testified as a general and case-specific nephrology expert witness in the bellwether trial, Fiorella Dial v. Fresenius Medical Care Holdings, Inc., et al., in February, 2017 before United States District Judge Douglas P. Woodlock. At that time he assured the jury that the "normal" pre-dialysis serum bicarbonate level for a dialysis patient is about 22 to 24 mEq/L and confirmed that such a level is his "target" range for his patients. On cross-examination at that trial, however, Dr. Borkan acknowledged that the Dial decedent's pre-dialysis serum bicarbonate laboratory value was 26 mEq/L before four of his monthly dialyses but that on three of those occasions, his bicarbonate level decreased to a reading of 22 to 24 mEq/L without any change in prescription. Dr. Borkan's expert report

on general causation defines "elevated" serum bicarbonate levels as greater than 26 mEq/L.

Drs. Fine, Waikar, Goldfarb and Borkan all rely on the data discussed in the Hakim Memo to support their opinions on general causation in their expert reports. Dr. Fine also relied on the Hakim Memo at his deposition for his opinion that alkalosis is a trigger when

> someone has an event on dialysis, a cardiopulmonary arrest or cardiac arrest, [and] in patients who are having cardiac events, they're more likely to have a high bicarbonate.

During his deposition, Dr. Goldfarb identified data in the Hakim Memo as "the data that's important" to support his opinion that "the increase in serum bicarbonate . . . was associated with an increase in sudden death." Dr. Borkan also testified that the Hakim Memo is the basis for some of his opinions.

3. Facts Applicable to All Causation Plaintiffs

As discussed above, the Hakim Memo sets forth Dr. Hakim's findings regarding the relative risk to dialysis patients of cardiopulmonary arrest and sudden cardiac death based on their pre-dialysis serum bicarbonate levels.

On December 1, 2014, Dr. Hakim testified that he would want a patient to sit for between 90 minutes and two hours before doing a post-dialysis bicarb draw because

> the ability . . . to metabolize bi-acetates is different in different patients. Some take longer; some take less time. But the data that I've seen is that it goes up up to 90 minutes after termination, and then it starts coming down again.

Plaintiffs' cardiology experts, Drs. Joseph G. Akar, Julian M. Aroesty, Zayd A. Eldadah, Joseph Shawn Miles, Arthur Z. Schwartzbard and Douglas Zipes all rely, at least in part, on the Hakim Memo to support their expert opinions on general causation. Dr. Miles, when asked what research he relied on to support his ultimate opinion, testified that he relied on "[t]he November 4, 2011 memo and prior Fresenius documents."

Dr. Akar's report opines that 1) "[c]omplex arrhythmias" require a trigger and an "underlying substrate that allows its perpetuation," 2) dialysis patients "are highly vulnerable to the development of arrhythmias in the setting of the alkalotic process and hypokalemia" which involves an "intracellular shifting of potassium," and 3) NaturaLyte and GranuFlo "produc[e] a process of alkalosis" that exposes patients to "an increased risk of cardiac arrest and death." The report further notes that rapid shifts in potassium levels during dialysis have been associated with sudden death. Thus,

> the more rapid and the greater the changes are in pH, the higher the gradients that are created, and the more rapid and steeper shifts in potassium levels.

During his June, 2015 deposition, Dr. Akar testified that GranuFlo and NaturaLyte

> have the potential to provide excess acetate, and this excess acetate has the potential to cause significant alkalosis, and alkalosis has the potential to . . . have a significant effect on ionic channels which has a potential to produce sudden cardiac death.

Dr. Akar noted that looking at the statistics with respect to sudden cardiac death around the time of dialysis, "0 to 12 hours is a particularly high period in which sudden cardiac death due to arrhythmias occurs."

Dr. Lucius M. Lampton, who submitted expert reports on behalf of plaintiffs Boyd, Carter, Clark, Dunaway, Dennis, McGhee, McNulty, Ross and Walker, attached and incorporated Dr. Akar's report by reference in his case-specific expert reports.

Dr. Aroesty's report opines that end-stage renal disease ("ESRD")

> patients have high comorbidity (e.g. diabetes, hypertension, atherosclerosis) making them particularly vulnerable to SCA/SCD [sudden cardiac arrest/sudden cardiac death] triggers

and that hypokalemia and alkalosis can be triggers for sudden cardiac arrest and sudden cardiac death. It further states that the

> change in dialysate formulation to include diacetate [in GranuFlo] was accompanied by a progressive increase in pre [hemodialysis] blood pH (i.e.

> alkalosis) [and] the incremental increase in pH (alkalosis) resulted in a shift of potassium (K) ions across the cell membrane with consequent increased risk of VT/VF [ventricular tachycardia/ventricular fibrillation] and SCA/SCD.

His report also notes that a rapid change in a patient's electrolyte and acid/base balance during hemodialysis is an additional risk factor for development of ventricular tachycardia/ventricular fibrillation and sudden cardiac arrest/sudden cardiac death.

Dr. Eldadah's report concludes that sudden "derangement" in serum potassium levels can cause "abnormal heart rhythms" that can be fatal and that

> sudden cardiac death or injury occurred in dialysis patients who received GranuFlo or NaturaLyte because these compounds cause: (a) an increased load of acetate in the body, which caused (b) an increased load of serum bicarbonate in the body (due to the conversion in the liver of acetate to bicarbonate), which caused (c) an acute drop in serum potassium concentrate, which caused (d) lethal cardiac arrhythmias.

Dr. Eldadah's report also states that "ventricular tachycardia and/or ventricular fibrillation" and sudden cardiac death can ensue from "rapid" changes in blood pH that "derange the orderly flow of electricity through the heart muscle."

Dr. Miles's report determines that higher concentrations of dialysate bicarbonate cause metabolic alkalosis, which causes hypokalemia, hypocalcemia and hypoxia and can result in

> shifts in potassium, calcium and oxygen [which] can cause sudden cardiac arrest and death, myocardial infarction and stroke.

Moreover, Dr. Miles's report states that "exposure to bicarbonate and acetate in the dialysate" during dialysis subjects patients to "rapid potassium shifting resulting in hypokalemia, which is a well-known cause of sudden cardiac death."

Dr. Schwartzbard's report postulates that elevated bicarbonate levels and low potassium concentrations can cause life threatening ventricular arrhythmias "in the susceptible ESRD population, leading to sudden cardiac arrest (SCA) and death (SCD)." The shift in bicarbonate leads to electrolyte disorders, such as hypokalemia and hypocalcemia, which cause an increased risk of cardiac arrhythmia. Dr. Schwartzbard explains that "[w]hen a patient who was previously well within an hour prior to his demise dies suddenly, the event is termed sudden cardiac death (SCD)."

Dr. Zipes's report theorizes that

> alkalosis due to elevated serum bicarbonate concentrate, . . . a low serum potassium concentration, . . . a combination of elevated serum bicarbonate concentration and low serum potassium concentrate, . . . rapid electrolyte shifts following administration of Granuflo [sic] and Naturalyte [sic], and . . . acidosis each can trigger life threatening ventricular arrhythmias in the susceptible ESRD dialysis patients, [which] can lead to cardiopulmonary arrest and death.

Dr. Zipes's report also notes that a "catastrophic arrhythmic event . . . is called sudden cardiac arrest (SCA) and leads to death unless reversed promptly." Dr. Zipes testified during his June, 2015 deposition that his understanding of this case is that there was a problem with the dialysate, here GranuFlo and/or NaturaLyte, that created a metabolic electrolyte imbalance resulting in sudden cardiac arrest and ultimately death.

4. Facts Applicable to NaturaLyte Plaintiffs

NaturaLyte and GranuFlo are acid concentrates used in the creation of dialysate, the dialysis solution. GranuFlo is a dry powder acid concentrate that contains various electrolytes, four mEq/L of sodium acetate and four mEq/L of acetic acid. Together, those two solutions form sodium diacetate. When combined with a bicarbonate concentrate and water, GranuFlo provides eight mEq/L of acetate to the dialysis solution. NaturaLyte, the subject of one of the four motions before the Court, is a liquid acid concentrate that contains various electrolytes and four mEq/L of acetic acid. When combined with a bicarbonate concentrate and water, NaturaLyte provides four mEq/L of acetate to the dialysis solution.

Fresenius facilities use those products in their dialysis procedures. It also sells and markets its products to other

dialysis facilities, including many clinics that compete with Fresenius facilities, such as DaVita Dialysis Centers, Dialysis Clinics Inc. and Renal Ventures Management LLC.

GranuFlo and NaturaLyte have been on the market for many years. The United States Food and Drug Administration ("FDA") cleared NaturaLyte for marketing in 1981 and, a decade later, cleared GranuFlo for marketing.[1] In the years since NaturaLyte was cleared for sale, other manufacturers of acid concentrates for hemodialysis have also offered a liquid product with four mEq/L of acetate and they continue to do so. Notably, the labels for other liquid acid concentrate products with four mEq/L of acetate identify the acetate contents in the same manner that the NaturaLyte label identified its acetate contents.

Fresenius sold over 305 million gallons of NaturaLyte in the United States between 2000 and 2012. NaturaLyte has been used in clinical settings since the early 1980s and has been used in hundreds of millions of hemodialysis treatments. Several of plaintiffs' experts, including Dr. Fine, Dr. Paul Miller and Dr. Waikar testified that they used NaturaLyte to treat their patients in a safe and effective manner.

[1] NaturaLyte and GranuFlo are regulated as medical devices by the FDA and are subject to FDA clearance rather than FDA approval.

5. Facts Applicable to Learned Intermediary Doctrine Plaintiffs

Fresenius's Chief Medical Office issued several memoranda, including the Hakim Memo discussed above, between 2000 and 2011 which discuss GranuFlo and NaturaLyte, acetate, acid/base balance, serum bicarbonate levels, alkalosis, the concept of "total buffer" and potential mortality and cardiac risks. Those memoranda were distributed to physicians and faculty staff as well as posted to the Fresenius Intranet website. The Hakim Memo was also sent to DaVita the same day that it was distributed to Fresenius physicians.

In March, 2012, Fresenius also issued an "Important Prescribing Information" notification to all known customers that had purchased GranuFlo or NaturaLyte. That notification stated, in part that

> NaturaLyte Liquid contributes 4.0 mEq/L of acetate and GranuFlo contributes 8.0 mEq/L of acetate to the final dialysate; which in addition to bicarbonate, combine to the total buffer that the patient receives from the dialysate. Acetate is also contained in the dialysis acid concentrates produced by other manufacturers. Since acetate is rapidly converted into bicarbonate by the liver, the bicarbonate prescription entered into the dialysis machine underestimates the total buffer that the patient receives from the dialysate by ~8 mEq/L with dialysate prepared from Granuflo (powder) or by ~4 mEq/L with dialysate prepared from NaturaLyte (liquid).

The notification recommended that physicians individualize prescriptions and "review[] them monthly with consideration of patient's pre-dialysis bicarbonate and dialysate total buffer."

Furthermore, plaintiffs' experts Drs. Goldfarb and Fine both testified that nephrology fellows know from medical school that acetate metabolizes into bicarbonate in the liver. Dr. Miller agreed, stating that

> most nephrologists who have been through high school and then college and then medical school, would understand that acetate converts in the body to bicarbonate.

Plaintiffs' experts also testified that NaturaLyte containers are labeled with the contents in the acid concentrate, including the acetate concentration.

B. Procedural Background

As relevant here, the plaintiffs against whom summary judgment is sought opted out of the global settlement agreement. Those plaintiffs are subject to the Lone Pine Order entered by United States District Judge Douglas P. Woodlock on January 26, 2017. Under that order, the opt-out plaintiffs were required to provide: 1) an affidavit by counsel that attested to the fact that counsel had reviewed documents or data supporting the contention that GranuFlo or NaturaLyte acid concentrate was used during the last dialysis treatment of the subject patient prior

to the alleged injury and 2) an affidavit executed by a qualified physician or other medical expert setting forth an opinion about specific causation. The plaintiffs were given until July 28, 2017 to decide whether to opt in to the settlement or comply with the Lone Pine Order.

Plaintiffs' operative pleading asserts claims for: 1) strict liability, 2) negligent failure to warn, 3) negligent design, 4) negligence, 5) negligent misrepresentation, 6) breach of implied warranty of merchantability, 7) breach of implied warranty of fitness for a particular purpose, 8) breach of express warranty, 9) fraud, 10) violation of consumer protection laws, 11) loss of consortium, 12) wrongful death and 13) survival actions.

In August and September, 2017, Fresenius filed four successive summary judgment motions as to the remaining opt-out plaintiffs. Judge Woodlock held oral argument on those summary judgment motions in November, 2017.

Plaintiff Josephine Gallardo Hernandez filed her complaint in January, 2018. Fresenius moved for summary judgment against her with respect to the issues of serum bicarbonate, causation and Naturalyte in January, 2019. Because Fresenius has incorporated by reference the facts and arguments set forth in its original four motions for summary judgment, the Court will

address that motion in conjunction with those affecting the other plaintiffs.[2]

This Multi-District Litigation was reassigned to this session of this district court in June, 2023. Upon reassignment, the assigned judicial officer held a status conference in July, 2023, to determine the status of the remaining cases. The Court ordered the parties to file status reports on or before August 17, 2023, to inform the Court as to any potential resolution of those cases.

Fresenius reported at the status conference and in its status reports that the summary judgment motions have been fully-briefed and all of the above-captioned cases are ripe for rulings on the merits by this Court. Counsel for plaintiffs Dunaway, Boyd, McNulty, Cameron, Carter, Clark, Dennis, Ross, Williams, Walker and McGhee protest only now in their status report that such plaintiffs do not agree that the cases are ripe for rulings on the merits. Those plaintiffs did not object at the July, 2023, status conference to this session deciding the fully-briefed motions for summary judgment nor have they even yet suggested why the cases are not ripe for decision.

[2] That motion for summary judgment is Docket No. 31 in Case No. 18-11224.

After careful consideration of all the briefs on file, the transcript of oral argument before Judge Woodlock and his extensive prior labor on the subject, the Court will allow defendants' pending motions for summary judgment.

II. Legal Standard

The role of summary judgment is "to pierce the pleadings and to assess the proof in order to see whether there is a genuine need for trial." Mesnick v. Gen. Elec. Co., 950 F.2d 816, 822 (1st Cir. 1991) (quoting Garside v. Osco Drug, Inc., 895 F.2d 46, 50 (1st Cir. 1990)). The burden is on the moving party to show, through the pleadings, discovery and affidavits, "that there is no genuine dispute as to any material fact and the movant is entitled to judgment as a matter of law." Fed. R. Civ. P. 56(a).

A fact is material if it "might affect the outcome of the suit under the governing law . . . ." Anderson v. Liberty Lobby, Inc., 477 U.S. 242, 248 (1986). A genuine issue of material fact exists where the evidence with respect to the material fact in dispute "is such that a reasonable jury could return a verdict for the nonmoving party." Id.

If the moving party satisfies its burden, the burden shifts to the non-moving party to set forth specific facts showing that there is a genuine, triable issue. Celotex Corp. v.

Catrett, 477 U.S. 317, 324 (1986). The Court must view the entire record in the light most favorable to the non-moving party and make all reasonable inferences in that party's favor. O'Connor v. Steeves, 994 F.2d 905, 907 (1st Cir. 1993). Summary judgment is warranted if, after viewing the record in the non-moving party's favor, the Court determines that no genuine issue of material fact exists and that the moving party is entitled to judgment as a matter of law.

III. Analysis

The Court addresses separately below the four successive summary judgment motions filed by Fresenius.

A. Serum Bicarbonate

Fresenius moves for summary judgment on the claims of ten plaintiffs with respect to the serum bicarbonate levels of the decedents. Fresenius asserts that it is entitled to summary judgment because 1) patients with bicarbonate levels below 28 mEq/L are outside the Hakim Memo's risk range and therefore there is a lack of evidence of medical causation and 2) the testimony of plaintiffs' experts shows that the alleged failure of Fresenius to warn could not proximately cause injury to patients with bicarbonate levels of 26 or lower.

Causation is an essential element for each of plaintiffs' claims. Plaintiffs are required to establish two kinds of

causation: general and specific. See In re Neurontin Mktg., Sales Practices, & Prods. Liab. Litig., 612 F. Supp. 2d 116, 123 (D. Mass. 2009). Specifically,

> [g]eneral causation is established by demonstrating, often through a review of scientific and medical literature, that exposure to a substance can cause a particular disease, [and specific causation] is established by demonstrating that a given exposure is the cause of an individual's disease.

Id. (citations omitted). Thus, plaintiffs must establish general causation by showing the drug's capacity to cause the injury generally and specific causation by showing "that the drug did cause the injury in this case." Kerlinsky v. Sandoz Inc., 783 F. Supp. 2d 236, 240 (D. Mass. 2011). Here, Fresenius argues that plaintiffs have failed to adduce any evidence to meet their burden of establishing both general causation and specific causation.

1. General Causation Theory

Fresenius's motion rests in part on the proposition that the Hakim Memo, on which all of plaintiffs' nephrology experts rely, demonstrates that plaintiffs' general causation theory is unavailing. That theory is that GranuFlo and NaturaLyte increase patients' serum bicarbonate to dangerous levels, which leads to alkalosis, which leads to cardiac arrest. The Hakim Memo, however, indicates that the heightened risk of cardiopulmonary arrest applies only to patients whose last pre-

dialysis lab results indicate a serum bicarbonate level of 28 mEq/L or greater or a potassium level of less than four mEq/L. Because none of the patients at issue here had a last pre-dialysis serum bicarbonate level that was 28 mEq/L or higher, Fresenius contends that no individual plaintiff is able to establish specific causation by virtue of the fact that none of them qualifies under the general causation theory. In fact, the range of levels recorded for plaintiffs' decedents is from 19 mEq/L to 26 mEq/L, all below the threshold established by the Hakim Memo.

Moreover, Fresenius notes that plaintiffs' general causation nephrology experts 1) conducted no independent studies on the alleged association between serum bicarbonate levels and the risk of cardiac arrest and 2) explicitly relied on the Hakim Memo in rendering their own opinions with respect to whether heightened serum bicarbonate levels cause alkalosis and, in turn, cardiac arrest.

The plaintiffs here, whose decedents' final pre-dialysis serum bicarbonate levels all fell below 28 mEq/L, do not qualify under their own core liability theory and they have adduced no evidence to support general causation.

a. The Plaintiffs' General Opposition

Plaintiffs cite portions of expert testimony selectively to support their theory but in essence they allege that dialysis can cause a spike in serum bicarbonate levels leading to alkalosis in any patient and alkalosis can cause sudden cardiac arrest and death. Plaintiffs cannot create an issue of fact by contorting or expanding their theory of general causation.

Plaintiffs' operative complaint, the Second Amended Master Complaint, is an administrative device filed with the intent of setting forth claims of the individual plaintiffs against Fresenius and plaintiffs are therefore bound by it. According to that complaint, acidosis is a typical occurrence for patients in kidney failure and severe acidosis can lead to shock or death. Dialysis attempts to correct an acidotic state by adding bicarbonate to the patient's blood. Acidosis is the opposite of alkalosis, which occurs when a patient's blood has excess base. Alkalosis is caused by too much bicarbonate in the blood and can cause cardiac arrhythmias and/or death. Thus, a purpose of dialysis is to add bicarbonate to a patient's blood to correct acidosis.

During dialysis, blood is pumped in one direction and the dialysate in the opposite direction. A nephrologist may order a particular dialysate solution containing specific amounts of

potassium, sodium, magnesium and calcium depending upon the patient's electrolyte balance. The dialysate solution used during dialysis is a mixture of a bicarbonate concentrate and acid concentrate. The bicarbonate concentrate is used on all dialysis patients, although the amount of bicarbonate can be adjusted. Because patients experiencing renal failure

> tend to become acidotic, and that problem is corrected primarily by adding bicarbonate to their blood . . . , all dialysate solutions contain bicarbonate to correct the naturally occurring acidosis in patients in renal failure.

GranuFlo and NaturaLyte are the acid concentrate portions of the dialysates at issue and when they are introduced into the body, the acetate within the acid concentrate is converted into bicarbonate by the liver, which increases bicarbonate levels in the blood. Because GranuFlo contains sodium diacetate, plaintiffs contend that the conversion in the liver produces an unanticipated amount of bicarbonate that exceeds what is normally and reasonably prescribed by the physician attending to the patient, leading to a higher "total buffer."

In sum, plaintiffs allege:

> a significant number of dialysis patients develop an unexpectedly rapid increase in elevated levels of bicarbonate in their blood during dialysis, as well as the potential for added serum bicarbonate post dialysis as the acetate in the blood continues to metabolize into bicarbonate. Patients with elevated bicarbonate levels in their blood suffer from metabolic alkalosis, the opposite of acidosis, and

> high bicarbonate levels in the blood increases a patient's risk of cardiopulmonary arrest ("CP") or sudden cardiac arrest.

Moreover, plaintiffs repeat that

> a dangerous increase in serum bicarbonate levels in patients undergoing hemodialysis . . . contributes to metabolic alkalosis, which is a significant risk factor associated with . . . heart arrhythmia, cardiopulmonary arrest and sudden cardiac death.

Throughout the complaint, plaintiffs focus on the allegation that "too much bicarbonate" can lead to levels "outside the normal or tolerated range" leading to alkalosis "(high blood pH)." Finally, plaintiffs make clear that Fresenius was aware that patients given GranuFlo had "higher than normal pre-dialysis bicarbonate levels" and "an increase in cases of metabolic alkalosis." Because Fresenius was aware that pre-dialysis serum bicarbonate levels that were "at or above 28 mEq/L" indicated a "20% increase in death risk," plaintiffs allege that Fresenius had a duty to warn and should have known their product was defective and dangerous.

Indeed, even plaintiffs' opposition relies on their Omnibus Memorandum in Support of General Causation, which makes clear that their theory of general causation is that excessive bicarbonate "total buffer" in the dialysate causes metabolic alkalosis, arrhythmia, sudden cardiac arrest and death. However, while purporting to be confined to that general theory

of causation, plaintiffs attempt to expand their theory to allege that any bicarbonate level pre-dialysis that is not between 22 and 24 mEq/L should cause concern to experts. They do that by relying on several experts, all of whom have slightly different ranges of serum bicarbonate levels that they consider "normal" or in the "target" range. Thus, plaintiffs cannot come to a consensus via their own experts as to what level of pre-dialysis serum bicarbonate is in a non-concerning range. Furthermore, none of their experts purported to change a prescription on numbers between 19 and 26 mEq/L and none testified that he or she was concerned about numbers on the low end because of alkalosis. Thus, plaintiffs have failed to set forth any competent evidence in support of their claims that essentially any pre-dialysis number comports with their theory of general causation.

Plaintiffs cite Dr. Goldfarb's testimony that bicarbonate levels below 22 mEq/L or 28 mEq/L and above would be concerning and therefore contend that decedents Boyd, Jenkins, McGhee and Myles, all of whom had pre-dialysis serum bicarbonate levels of 19 or 20, have created a genuine issues of material fact precluding summary judgment. At best, however, plaintiffs have proffered evidence that acidosis is of concern to doctors. Acidosis is the opposite of alkalosis and although it may be

disconcerting, it does not support the general causation theory plaintiffs have advanced.

Next, plaintiffs rely on Dr. Fine's testimony that he likes to "see the bicarb[onate] somewhere between, in most cases, 20 and 24 mEq/L." on that basis, they contend that decedents McNulty, Ross and Hughes, all of whom had pre-dialysis serum bicarbonate levels of 25 or 26 mEq/L, have adduced sufficient evidence to preclude summary judgment. Plaintiffs refer to Dr. Waikar's testimony that his target range is 22 mEq/L to 24 or 26 mEq/L and that the presence of chronic obstructive pulmonary disease ("COPD") might lead him to adjust the bicarbonate prescription for a patient. They claim, on that basis, that Ms. Cothern and Ms. Carter, both of whom had COPD, have raised a genuine issue of material fact. Dr. Waikar, however, testified clearly that COPD might lead him to increase the amount of bicarbonate in the dialysate, i.e. he would seek to elevate their serum bicarbonate levels. That treatment would have caused more serious electrolyte shifts and alkalosis in patients and, accordingly, the Court perceives no genuine issue of material fact created thereby and the argument that Ms. Cothern and Ms. Carter had COPD is irrelevant to plaintiffs' theory.

On behalf of Ms. Boyd, Mr. Jenkins, Mr. McGhee and Ms. Myles, plaintiffs contend that, because their pre-dialysis serum

bicarbonate levels were all 19 mEq/L, they are outside the range indicated as Dr. Waikar's target. But, pursuant to Dr. Goldfarb's opinion that low numbers are of concern, such levels, which reflect acidosis, are inconsistent with plaintiffs' theory of general causation.

Finally, plaintiffs cite Dr. Borkan's testimony that he would not dial back the bicarbonate level unless the patient had a pre-dialysis reading that is above 24 mEq/L. They interpret that to mean that Dr. Borkan would necessarily reduce the bicarbonate level if the reading were above 24 mEq/L. But Dr. Borkan's prior testimony does not support that conclusion. He testified during the Dial trial that it was the number 28 mEq/L that constituted a "trigger" for alkalosis. He did not discuss 26 mEq/L, 19 mEq/L or any number in between in articulating his opinion during Dial. Indeed, he has testified that serum bicarbonate levels of 26 mEq/L can adjust on their own, without a change in prescription. Furthermore, despite evidence that the Dial plaintiff had multiple readings of 26 mEq/L while she was on dialysis, Dr. Borkan did not testify that such a reading was of concern.

Dr. Borkan's ambiguous testimony cannot, standing alone, create a genuine issue of material fact. Although plaintiffs are not necessarily bound by the Hakim Memo, it is relevant in

assessing their theory of causation, not least because their experts all explicitly purported to rely on it in rendering their opinions. Without any definitive expert testimony regarding what is normal but with considerable testimony from their own experts that all of the plaintiffs fell within an acceptable range, they have failed to adduce competent evidence in support of their claims.

b. Plaintiff Riben's Opposition

The plaintiffs who joined in Riben's opposition argue that Fresenius has read their theory of causation too narrowly and that any pre-dialysis bicarbonate level, low or high, could still lead to a cardiac event solely based on the administration of a high-bicarbonate dialysate. More directly, plaintiffs attempt to advance a theory that it is the shift caused by a high-bicarbonate dialysate alone, regardless of the "total buffer," which is important. They seek to divorce the "rapid shift" from the alkalosis itself.

Such an expansion of their theory is not, however, articulated in the Second Amended Master Complaint, nor is it supported by expert testimony. Even more problematic for the plaintiffs who purport to join the Riben opposition, they clearly explain in their own opposition that their theory of general causation is

> that excessive bicarbonate "total buffer" . . . in the "dialysate" . . . is capable of causing metabolic alkalosis, arrhythmia, sudden cardiac arrest (SCA), and death.

Moreover, as Fresenius points out, if plaintiffs' new theory of causation is that dialysis can dramatically increase serum bicarbonate in a short period of time, separate from total buffer levels, it is related to the dialysis process itself and not the dialysates used. Thus, such an attempt to re-frame the theory of general causation is unavailing.

2. Proximate Cause Issues

Fresenius next argues that the testimony of plaintiffs' own experts indicates that its purported failure to warn could not proximately cause injury to patients who had serum bicarbonate levels of 26 mEq/L and lower. For example, plaintiffs' experts testified that a physician would not be expected to make a downward adjustment to the bicarbonate setting of a patient with a reading of 26 mEq/L or lower. According to Fresenius, that means plaintiffs have failed to establish a proximate cause linking the alleged failure to warn to the alleged injuries.

To prevail on any failure to warn claim, plaintiffs must show that the lack of warning was the proximate cause of their decedents' injuries. Santos-Rodriguez v. Seastar Solutions, 858 F.3d 695, 697 (1st Cir. 2017). Thus, plaintiffs must show that the treating doctors would have done something differently had

they been forewarned as plaintiffs claim they should have been. See, e.g., In re Neurontin Mktg. & Sales Practices & Prods. Litig., No. 04-CV-10981-PBS, 2010 WL 3169485, at *3-4 (D. Mass. Aug. 10, 2010) (noting that "[w]here the manufacturer fails to provide the physician with an adequate warning, courts have held that the manufacturer may still be shielded from liability if it can show that the prescribing physician would not have heeded an adequate warning").

In this case, plaintiffs' experts have testified that pre-dialysis serum bicarbonate readings of 26 mEq/L and lower do not require prescription changes. In particular, Dr. Waikar testified that a range of 22 to 26 mEq/L was "reasonable," Dr. Goldfarb testified that he would be concerned about serum bicarbonate levels that are at "28 or 30 or 35" mEq/L or below 22 mEq/L, and Dr. Fine testified that he asks his nurse practitioners to let him know if the serum bicarbonate levels of a patient are above 26 mEq/L. Furthermore, Dr. Fine declared that he does not find it necessary to adjust a bicarbonate prescription downward unless the patient is "alkalotic" or if the patient's serum bicarbonate levels had drastic upward swings in a short period of time.

Although Dr. Borkan averred that he would consider making adjustments for his own patients when their serum bicarbonate

levels exceeded 24 mEq/L, he also attested that he considered 28 mEq/L to be a "trigger" for alkalosis and that a patient's multiple prior readings of 26 mEq/L decreased on their own without any change in prescription, indicating that he did not believe a reading of 26 mEq/L necessarily required a prescription change. Plaintiffs whose decedents had pre-dialysis serum bicarbonate readings of 26 mEq/L or below and who had no indications of drastic upward swings in a short period of time have adduced no evidence to support their claims that any of their treating doctors would have done anything differently.

On the question of proximate cause, it is clear that plaintiffs could pick and choose among their experts one who might say that their pre-dialysis serum bicarbonate numbers are troubling but few of them fall into the category that would have been of concern to any of the experts with respect to alkalotic problems. Only plaintiffs McNulty, Ross and Williams were in a range that any of the experts indicated would have warranted notification. None of plaintiffs' experts has testified that he or she would be inclined to change the dialysate based on a pre-dialysis serum bicarbonate level of 25 or 26 mEq/L and most of those experts have said that those numbers fall within their "target range." Plaintiffs are not bound by the Hakim Memo but they were required to produce some reliable evidence to create genuine issues of material fact as to whether their pre-dialysis

serum bicarbonate levels were too high and would lead a doctor to change the dialysate prescription. They have not done so.

B. Causation

Fresenius's second motion for summary judgment contends that it is entitled to summary judgment against 11 opt-out plaintiffs because 1) those plaintiffs have not shown that their decedents died as a result of arrhythmia and 2) the decedents' injuries are not proximate in time to their last dialysis treatments. Essentially, Fresenius contends that plaintiffs' theory of general causation rests on the fact that the dialysates cause alkalosis, which leads to an arrhythmia "triggered" by an electrolyte shift. Therefore, plaintiffs must demonstrate the "right event type" in order to elicit sufficient evidence to meet their burden. Moreover, Fresenius argues that an arrhythmia can only be attributed to the acid concentrate in the dialysate if it occurs within two hours after the dialysis treatment concludes.

As indicated with respect to the serum bicarbonate motion, plaintiffs are required to establish causation, both general and specific. See In re Neurontin Mktg., 612 F. Supp. 2d at 123. Furthermore,

> as is well-established under Massachusetts law, "expert testimony is required to establish medical

> causation." This applies to both general and specific causation.

Milward v. Rust-Oleum Corp., 820 F.3d 469, 476 (1st Cir. 2016) (quoting Reckis v. Johnson & Johnson, 28 N.E.3d 445, 461 (Mass. 2015)). If there is no evidence regarding general causation, then "judgment as a matter of law [is] necessarily required." Id.

1. Event Type

Fresenius's first argument is based on the Hakim Memo in which Dr. Hakim made no mention of sepsis, blood clots, myocardial infarction or anything aside from electrolyte-related arrhythmias. Because plaintiffs' claims are premised almost entirely on Fresenius's failure to warn of the electrolyte-related arrhythmias (which can lead to sudden cardiac arrest and death), Fresenius contends that any other event is outside the scope of this litigation.

Fresenius next asserts that the theory of general medical causation espoused by plaintiffs requires proof that the decedents' injuries were caused by a cardiac arrhythmia triggered by an electrolyte shift. Therefore, non-cardiac events and cardiac events

> that are not arrhythmic . . . or that involve arrhythmias due to triggers other than electrolyte shifts

do not fall within the scope of this litigation.

The decedents of the following plaintiffs have medical records indicating that cause of death was something other than alkalosis leading to arrhythmia: Daniel Carter, Kathy Dennis, Max Riben and Sophia Walker. In fact, the decedents of plaintiffs Carter and Walker suffered from sepsis, which led to either cardiac arrest or to septic shock and neither experienced arrhythmia. The decedents of plaintiffs Dennis and Riben died as a result of myocardial infarction.

2. Timing

Fresenius next submits that plaintiffs have failed to establish that the timing of the alleged injury events were in close proximity to the patients' last dialysis treatments. In particular, Fresenius challenges the claims of plaintiffs Boyd, Carter, Clark, Dunaway, McGhee, McNulty and Ross.

Fresenius argues that the Hakim Memo relates solely to in-center cardiac arrests and that plaintiffs' cardiology experts testify that it is "rapid" electrolyte shifts during dialysis that trigger arrhythmia, which occurs suddenly once triggered. None of the seven identified plaintiffs experienced in-center cardiac arrest and all of the cardiac arrests occurred seven hours or more after the conclusion of dialysis: plaintiff Boyd's decedent (19 hours), plaintiff Carter's decedent (36 hours),

plaintiff Clark's decedent (31 hours), plaintiff Dunaway's decedent (45 hours), plaintiff Gallardo Hernandez's decedent (8 days), plaintiff McNulty's decedent (30 hours), plaintiff McGhee's decedent (8.5 hours) and plaintiff Ross's decedent (8.5 hours).

Plaintiffs' general causation expert, Dr. Akar, identified the "0 to 12 hour" interval after dialysis as "a particularly high period in which sudden cardiac death due to arrhythmias occur." Despite that 0-to-12 hour interval, however, Dr. Akar concluded that the acetate converts to bicarbonate in the body instantaneously so that any electrolyte shifting happens "within minutes, probably even less than minutes." In essence, any elevation in bicarbonate, which would "trigger" arrhythmia, occurs almost immediately, either during dialysis or perhaps right afterward.

The only potential issue plaintiffs raise results from the opinion of Dr. Borkan that certain patients metabolize acetate more slowly such that the blood bicarbonate level would "spike" and cause acute metabolic alkalosis hours after the end of dialysis. Based on that opinion, plaintiffs whose decedents experienced the alleged injury event more than 40 hours after dialysis have elicited sufficient evidence to create a genuine

issue of material fact as to whether the acetate in the dialysate solution caused the injuries.

Dr. Borkan's opinion is largely unsupported by the evidence, including the studies on which he purports to rely. The only study that arguably supports his theory regarding slow metabolizing of acetate is the one referenced in plaintiffs' opposition, the "Graham Study," which Fresenius attached to its reply brief.

The Graham Study, apparently undertaken out of concern for minimizing the effects of acidosis in hemodialysis patients, provides some support for the theory that a dialysate bicarbonate solution used to elevate the level of serum bicarbonate during dialysis might have an effect on bicarbonate values for as long as 44 hours.

The Graham Study sought to address the problem of acidosis in patients undergoing hemodialysis, the method of correcting it and the consequence of failing to do so. Essentially, the study monitored nine hemodialysis patients from just after dialysis to just before a subsequent dialysis 44 hours later. Seven out of the nine patients experienced "a gradual decline in bicarbonate, whilst in two there was no change." The study did not determine whether it was acetate that led to the elevated serum bicarbonate level but concluded that a slow linear decline in

bicarbonate after dialysis occurred in seven of the nine patients and that in eight of the nine, the average of their post- and pre-dialysis bicarbonate "accurately predicted the time-averaged . . . bicarbonate concentration." The study also looked at the post- and pre-dialysis serum bicarbonate levels of 46 other patients and found that the serum bicarbonate values were significantly lower three days after dialysis. The study did not determine why two patients remained steady in their bicarbonate numbers post- and pre-dialysis.

From that study Dr. Borkan concludes that

> there are probably a subset of patients who we send home from the dialysis unit with substantial metabolic alkalosis that persists for as long as until the next dialysis session.

But Dr. Borkan's conclusion based on the Graham Study still fails to support his delayed bicarbonate "spike" theory upon which plaintiffs apparently rely to claim that NaturaLyte and/or GranuFlo caused their decedents' alleged injury events.

Dr. Borkan's theory of delayed acetate to bicarbonate conversion due to slower metabolism ultimately rests on the idea of a "bicarbonate spike" that occurs after the completion of dialysis. That spike, because of excess acetate, occurs at a time attenuated from the dialysis itself and, according to Dr. Borkan,

> the timing of the spike is a key determinant of the toxic effects of acute metabolic alkalosis including [cardiopulmonary arrest] and death both during and after the procedure.

That "spike" theory is, however, unsupported by any of the evidence, including the Graham Study. At best, the Graham Study included two patients whose serum bicarbonate levels after dialysis remained constant. Neither of those two outliers had a belated "spike" in their serum bicarbonate levels.

Furthermore, multiple studies cited by Dr. Borkan show that acetate levels drop quickly soon after dialysis is completed and he himself testified during the Dial bellwether trial that "most patients" clear any residual acetate left in their blood from dialysis "within 30 to 60 minutes."

Moreover, there is no evidence in the record that any of the decedents at issue were slow to metabolize acetate. Where a single expert among many testifies that it is possible that some patients, although certainly not the majority, may take more than one hour after dialysis to clear the acetate from their blood that is not enough to create a genuine issue of material fact. Furthermore, there is no evidence that such was the case for these particular plaintiffs and the Graham Study did not even purport to be about acetate exclusively or to show the requisite bicarbonate "spike."

C. Naturalyte

Fresenius moves for summary judgment on the claims of five plaintiffs involving NaturaLyte, arguing that the admissions of Dr. Borkan and plaintiffs' other experts and the outcome in the bellwether trial, Dial, demonstrate that general causation is non-existent in any NaturaLyte case.

Once again, causation is a fundamental element of plaintiffs' claims and "to prevail in a pharmaceutical personal injury case," they must proffer evidence of both general and specific causation. See Jackson v. Johnson & Johnson & Janssen Pharms., Inc., 330 F. Supp. 3d 616, 625 (D. Mass. 2018) (quoting In re Neurontin Mktg., 612 F. Supp. 2d at 123). As an initial matter, general causation is

> established by demonstrating, often through a review of scientific and medical literature, that exposure to a substance can cause a particular disease.

In re Neurontin Mktg, 612 F. Supp. 2d at 123. As discussed above with respect to the causation motion, in Massachusetts, understanding medical causation is

> a matter beyond the common knowledge of the ordinary layman and proof of it must rest upon expert medical testimony.

Jackson, 330 F. Supp. 3d at 625 (quoting Hachadourian's Case, 340 Mass. 81, 84, 162 N.E.2d 663 (1959)).

Although Dr. Borkan endorses plaintiffs' allegations that NaturaLyte is dangerous and defective due to the fact that it contains four mEq/L of acetate, his own testimony and practices demonstrate that such a charge is unsubstantiated. On numerous occasions, as outlined above, Dr. Borkan testified that four mEq/L of acetate is not considered excess acetate. He testified that his own clinic uses a NaturaLyte product and that he does not warn his patients of that fact because the amount of acetate contained in the solution, i.e., four mEq/L, is an acceptable amount. Furthermore, during his trial testimony in Dial, Dr. Borkan reaffirmed his prior admission that four mEq/L of acetate is an "average, background" and "baseline" amount for an acid concentrate.

Besides Dr. Borkan's admission, several other experts retained by plaintiffs confirmed that NaturaLyte or some other solution containing four mEq/L of acetate is used in their clinics. Drs. Fine and Miller testified that they treated their dialysis patients with NaturaLyte. Dr. Miller confirmed that NaturaLyte is "a fine product" and contained the "standard amount" of acetate. Drs. Waikar and Goldfarb testified that the clinics where they treat their dialysis patients use a solution that contains four mEq/L of acetate, the same amount of acetate contained in NaturaLyte. Taking the evidence in the light most favorable to the nonmoving party, the Court discerns no manner

in which a reasonable jury could resolve the general causation issue in favor of plaintiffs.

Moreover, to defeat a motion for summary judgment, plaintiffs' "expert opinion[s] must be more than a conclusory assertion about ultimate legal issues." Hayes v. Douglas Dynamics, Inc., 8 F.3d 88, 92 (1st Cir. 1993). Plaintiffs' experts Drs. Aroesty, Akar and Lampton opine that excess acetate in NaturaLyte does indeed increase the risk of cardiac arrest and death. As discussed above, Dr. Lampton's reports for all of the decedents are conclusory, in that they merely recount Dr. Akar's conclusions. Similarly, Drs. Aroesty and Akar lump GranuFlo and NaturaLyte together when discussing the alleged excess acetate in the solutions, suggesting that both GranuFlo and NaturaLyte caused the alleged injuries. Such a bare conclusion does not create a genuine issue of material fact, particularly in the face of admissions from other experts indicating that they use products that contain four mEq/L of acetate with their own dialysis patients. As such, plaintiffs have produced no competent evidence contrary to what Fresenius has provided regarding the amount of acetate included in NaturaLyte and thus defendants' motion for summary judgment on plaintiffs' claims involving NaturaLyte will be allowed.

D. Learned Intermediary Doctrine

Finally, Fresenius argues that all 13 remaining plaintiffs' claims are barred by the learned intermediary doctrine because there can be no dispute that the prescribing physicians were adequately forewarned. The Court agrees.

Plaintiffs' claims are fundamentally grounded in the assertion that Fresenius failed to warn them of the dangers of NaturaLyte and/or GranuFlo. Pursuant to the learned intermediary doctrine, however, the prescribing physician is the relevant audience for warnings about a medical device or prescription drug. Garside v. Osco Drug, Inc., 976 F.2d 77, 80 (1st Cir. 1992) ("Where the product is a prescription drug, however, it is widely accepted that the manufacturer's duty to warn runs to the physician rather than the patient."); see also Plourde v. Sorin Grp. USA, Inc., 517 F. Supp. 3d 76, 89 (D. Mass. 2021). Thus, once Fresenius adequately warned the physicians providing the dialysis treatments, its duty to warn was fulfilled. See Garside, 976 F.2d at 80.

Fresenius contends that for plaintiffs in at least three sets of common circumstances, the record indisputably demonstrates that physicians were adequately warned. Those three groups of plaintiffs include: 1) those who received dialysis treatments preceding their alleged injury at a

Fresenius dialysis unit at any time, 2) those who received dialysis treatments preceding their alleged injury at a DaVita dialysis unit after November 4, 2011 and 3) those who received dialysis treatments preceding their alleged injury at any dialysis unit after March 29, 2012.

As explained in the fact section above, physicians and facility staff at Fresenius dialysis units were provided several memoranda from the Fresenius Chief Medical Office over the course of a decade. The memoranda are adequate warnings as a matter of law because they specifically mention the circumstances complained of. They repeatedly cautioned that total buffer is the sum of the acetate and bicarbonate and that acetate, once in contact with a patient's blood, is metabolically converted into bicarbonate. Specifically, the memoranda urged physicians to

> [o]bserve and monitor the patient's serum bicarbonate level to determine that the prescribed dialysate bicarbonate is actually being delivered and is appropriate for that particular patient. If not, the physician should establish a new bicarbonate prescription and the staff should readjust the bicarbonate setting as is appropriate.

Because the unrefuted evidence demonstrates that Fresenius provided adequate warnings, it has discharged its duty and summary judgment will be allowed, regardless of how the physicians responded to those warnings.

With respect to patients treated at DaVita clinics, including the decedent of plaintiff Riben, there is no dispute that DaVita clinics received the Hakim memo the same day it was released to Fresenius physicians, November 4, 2011. Plaintiff Riben's decedent suffered her injuries after that date. By the time of her injuries, DaVita clinics had already been well informed of the warnings for NaturaLyte and GranuFlo and as such, her attending nephrologists were also aware of the dangers of the products.

In the third category, the decedents of plaintiffs Cameron, Riben, Gallardo Hernandez, Walker and Williams all suffered injuries after the distribution of the March 29, 2012 "Important Prescribing Information" notification. That warning specifically addressed the matters of which the plaintiffs complain and, accordingly, it cannot be disputed that such a warning was adequate.

Finally, it does not escape the Court that there was testimony from nephrology experts indicating that nephrology fellows know from early on in medical school that acetate metabolizes into bicarbonate in the liver. Plaintiffs claim that prescribing physicians were unaware of such information and needed to be informed of it via warnings. Fresenius has proffered evidence, including testimony from plaintiffs' own

experts, that all competent nephrologists understand that acetate converts to bicarbonate and can read the labels on the products and see that they contain acetate. Plaintiffs, on the other hand, have failed to produce any evidence to show that physicians would have changed their prescribing decisions if different disclosures had been made. Therefore, a reasonable jury could not resolve such an issue in favor of plaintiffs and summary judgment for defendants will be allowed on the basis of the learned intermediary doctrine.

ORDER

For the reasons outlined above, defendants' motions for summary judgment on the claims of opt-out plaintiffs with respect to:

1) NaturaLyte (Docket No. 1906) is **ALLOWED;**

2) elevated serum bicarbonate levels (Docket No. 1913) is **ALLOWED;**

3) the learned intermediary doctrine (Docket No. 1923) is **ALLOWED;** and

4) non-arrythmia events or injuries not proximate in time to the last dialysis (Docket No. 1933), is **ALLOWED.**

Defendants' motion for summary judgment in Case No. 18-11224, with respect to plaintiff Gallardo Hernandez (Docket No. 31) is **ALLOWED.**

Accordingly, the cases brought by plaintiffs Dunaway, Boyd, McNulty, Cameron, Carter, Clark, Dennis, Ross, Williams, Walker, McGhee, Riben and Gallardo Hernandez are **DISMISSED**.

So ordered.

/s/ Nathaniel M. Gorton
Nathaniel M. Gorton
United States District Judge

Dated: September 7, 2023